

CLAIMS

That which is claimed is:

- 5 1. A method for producing a chemically-modified compound, said method comprising:
- (a) providing a compound bearing one or more water-soluble protecting groups, said water-soluble protecting group comprising a water-soluble polymer; and
- 10 (b) replacing one or more of said water-soluble protecting groups of said compound with a chemical adduct to form a chemically-modified compound.
- 15 2. The method of claim 1, wherein said compound is selected from the group consisting of a lipid, carbohydrate, nucleic acid, amino acid, peptide, polypeptide, protein and synthetic polymer.
- 20 3. The method of claim 1, wherein said chemical adduct is selected from the group consisting of a lipid, carbohydrate, nucleic acid, amino acid, peptide, polypeptide, protein and synthetic polymer.
- 25 4. The method of claim 1, wherein said water-soluble protecting group is attached to said compound through a cleavable linker.
5. The method of claim 4, wherein said cleavable linker comprises a covalent bond that is displaceable by said chemical adduct.
- 30 6. The method of claim 5, wherein said covalent bond is selected from the group consisting of oxime, hydrazone, diol, thioester, selenoester and disulfide.
7. The method of claim 5, wherein said chemical adduct comprises a reactive functional group capable of displacing said water-soluble protecting group.

8. The method of claim 7, wherein said reactive functional group is selected from the group consisting of aminooxy, diol, aldehyde, ketone, hydrazide, thiol, and selenol.

5 9. The method of claim 1, wherein said water-soluble protecting group comprises a repeat unit comprising a polyalkylene oxide, a polyamide alkylene oxide, or derivatives thereof.

10 10. The method of claim 9, wherein said polyalkylene oxide and polyamide alkylene oxide comprise an ethylene oxide repeat unit of the formula $-(CH_2-CH_2-O)-$.

15 11. The method of claim 1, wherein at least one of said water-soluble protecting groups is linear.

12. The method of claim 1, wherein said water-soluble protecting group comprises a net charge under physiological conditions selected from the group consisting of positive, neutral and negative.

20 13. The method of claim 1, wherein said water-soluble protecting group is mono-disperse.

14. The method of claim 1, wherein said compound is mono-disperse.

25 15. The method of claim 1, wherein said chemically modified compound is mono-disperse.

30 16. The method of claim 1, wherein said compound comprises two or more water-soluble protecting groups.

17. The method of claim 16, wherein said water-soluble protecting groups are joined to said compound through the same linkages.

18. A method of producing a library of chemically-modified compounds, said method comprising:

- 5 (a) providing a compound bearing one or more water-soluble protecting groups, said water-soluble protecting group comprising a water-soluble polymer;
- (b) splitting said compound into first and second reaction systems; and
- 10 (c) replacing one or more of said water-soluble protecting groups of said compound in said first reaction system with a first chemical adduct to form a first chemically-modified compound, and, optionally, replacing one or more of said water-soluble protecting groups of said compound in said second reaction system with a second chemical adduct to form a second chemically-modified compound, wherein said first and second chemical adducts are different.

15 19. A method of producing a chemically-modified ligated polypeptide chain, said method comprising:

- 20 (a) providing a first peptide segment bearing one or more water-soluble protecting groups, said water-soluble protecting group comprising a water-soluble polymer;
- (b) chemically ligating said first peptide segment to a second peptide segment to form a ligated polypeptide chain bearing one or more of said water-soluble protecting groups; and
- 25 (c) replacing one or more of said water-soluble protecting groups with a chemical adduct to form a chemically-modified ligated polypeptide chain.

30 20. The method of claim 19, wherein said first and second peptide segments comprise non-overlapping amino acid sequences of said polypeptide chain.

21. The method of claim 19, wherein said polypeptide chain comprises an amino acid sequence of a protein, and which further comprises folding said polypeptide chain to form a protein.

22. The method of claim 19, wherein one or more of said peptide segments are partially protected with protecting groups other than said water-soluble protecting group.

5 23. The method of claim 19, wherein one or more of said peptide segments are unprotected other than with said water-soluble protecting group.

10 24. The method of claim 19, wherein said chemically ligating comprises a chemoselective ligation chemistry selected from native chemical ligation, extended native chemical ligation, pseudo native chemical ligation, oxime forming chemical ligation, hydrazone forming chemical ligation, oxazolidine forming chemical ligation, thiazolidine forming chemical ligation, and thioester forming chemical ligation.

15 25. A method of producing a library of chemically-modified ligated polypeptide chains, said method comprising:

(a) providing a first peptide segment bearing one or more water-soluble protecting groups, said water-soluble protecting group comprising a water-soluble polymer;

20 (b) chemically ligating said first peptide segment to a second peptide segment to form a ligated polypeptide chain bearing one or more of said water-soluble protecting groups;

25 (c) splitting said ligated polypeptide chain into first and second reaction systems; and

30 (d) replacing one or more of said water-soluble protecting groups of said ligated polypeptide chain in said first reaction system with a first chemical adduct to form a first chemically-modified ligated polypeptide chain, and, optionally, replacing one or more of said water-soluble protecting groups of said ligated polypeptide chain in said second reaction system with a second chemical adduct to form a second chemically-modified ligated polypeptide chain, wherein said first and second chemical adducts are different.

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26. A kit comprising first and second containers, said first container comprising a compound bearing one or more water-soluble protecting groups, said water-soluble protecting group comprising a water-soluble polymer, said second container comprising a chemical adduct capable of replacing one or more of said water-soluble protecting groups of said compound in said first container.